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| 09/980,492 | 12/04/2001 | Rango Dietrich | 24826 | 6447 |

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NATH & ASSOCIATES PLLC
1030 FIFTEENTH STREET, N.W.
SIXTH FLOOR
WASHINGTON, DC 20005

| EXAMINER | |
|---|---|
| SHEIKH, HUMERA N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | 13 |

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/980,492 | Applicant(s) DIETRICH ET AL. | |
|---|---|---|---|
| | Examiner Humera N. Sheikh | Art Unit 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 4-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### Status of the Application

Receipt of the Request for Continued Examination (RCE) under Rule 1.114 and the Amendment, both filed 09/30/03 is acknowledged.

Claims 1, 2 and 4-47 are pending. Claims 1, 2, 11, 12, 15-18 and 20 have been amended. Claim 3 has been cancelled by virtue of the amendment. Claims 1, 2 and 4-47 are rejected.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1, 2 and 4-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama *et al.* (US Pat. No. 5,948,773) in view of Shell *et al.* (US Pat. No. 5,972,389).**

Akiyama *et al.* teach a pharmaceutical formulation comprising an antibacterial substance and/or an anti-ulcer substance, in that the anti-ulcer substance is a proton pump inhibitor, wherein at least either one of them is formulated into a gastrointestinal mucosa-adherent solid preparation, which comprises a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids) in combination with pharmaceutically acceptable excipients (see reference column 2, line 16 through col. 3, line 67); (col. 9, line 20 through col. 13, line 59).

The anti-ulcer substance includes H2 blockers and proton pump inhibitors, wherein proton pump inhibitors are preferred. The proton pump inhibitors include benzimidazole compounds such as *lansoprazole, timoprazole, omeprazole and pantoprazole*, for example (col. 3, lines 55-67; col. 9, lines 20-34). The salt of a benzimadole compound is preferably used as a physiologically acceptable salt. Physiologically acceptable salts include salts with *inorganic bases*, salts with organic bases and salts with basic amino acids (col. 9, lines 39-49).

The formulation of the invention is used as (1) a combination of an anti-ulcer substance and a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance, (2) a combination of an antibacterial substance and a gastrointestinal mucosa-adherent solid preparation containing an anti-ulcer substance, (3) a gastrointestinal mucosa-adherent solid preparation containing both an antibacterial substance and an anti-ulcer substance, or (4) a combination of a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance and a gastrointestinal mucosa-adherent solid preparation containing an anti-ulcer substance. The combination of an anti-ulcer substance and a gastrointestinal mucosa-adherent solid preparation containing an antibacterial substance is preferred (col. 9, lines 53-67).

Akiyama teaches that the matrix containing a polyglyerol fatty acid ester may also incorporate a lipid. The lipid is a water-soluble substance that serves to control the dissolution rate of active ingredients, exemplified by the previously mentioned lipids (col. 13, lines 12-16).

Regarding the use of the specified solid paraffin, Akiyama teaches the generic concept of adding hydrocarbons, such as paraffins, and thus would include various types of paraffin as those instantly claimed.

With respect to the specified triglyceride (i.e., tristearate, tripalmitate, trimyristate) and fatty acid ester (cetyl palmitate), Akayima recognizes the incorporation of triglycerides, such as monopalmitin and fatty acid esters, such as polyglycerin fatty acid esters of any type. The solid preparation may incorporate additives that include excipients, such as lactose, corn starch, talc, crystalline cellulose; binders, such as

sucrose, methyl cellulose, polyvinylypyrrolidone, etc; disintegrating agents, wetting agents, stabilizers and the like (col. 13, lines 28-52).

Example compositions for oral administration include various forms, such as tablets, pills, granules, powders, capsules, syrups, emulsions and suspensions. The granules taught by Akiyama have a particle size of up to approximately 1400 microns.

These compositions are produced by known methods, using lactose, starch, sucrose, magnesium stearate and other substances as carriers or excipients (col. 17, lines 25-29).

Akiyama, as noted above teaches various forms for administration (i.e., tablets, capsules, pills, powders, etc.). Akiyama does not teach that the active compound units are *microspheres.* One of ordinary skill in the art would be capable of determining any suitable dosage form for the delivery of drugs. Such skill is evident from the reference of Shell et al. (see below).

**Shell *et al.*** teach gastric-retentive oral drug dosage forms for the controlled release and delivery of sparingly soluble drugs, insoluble particulate matter from which drugs are released and soluble drugs rendered sparingly soluble when combined with a drug modifier, wherein the dosage forms are in the form of tablets, capsules and microparticulate systems of (proteinoid) microspheres. The dosage forms are useful for delivering drugs to treat local disorders of the stomach, such as those for eradicating Helicobacter pylori, stomach and duodenal ulcers, gastritis, esophagitis and gastric carcinoma. Suitable drugs that are delivered through these dosage forms include

antibiotics and gastric acid lowering agents, such as omeprazole (see reference column 1, line 45 – col. 6, line 55) and claims.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teachings of Shell *et al.* within the teachings of Akiyama because Shell teaches a gastric-retentive oral drug composition for treating disorders of the stomach (i.e., *h. pylori*, *ulcers, gastritis*) in dosage forms of tablets, capsules and microspheres, which provide advantageous properties of protecting the drug from the detrimental environment of the G.I. tract, enhancing drug absorption and altering drug solubility and similarly Akiyama teaches a gastrointestinal mucosa-adherent preparation for treating *h. pylori and ulcers* wherein the dosages include tablets, capsules, granules and the like. The expected result would be an improved proton pump inhibiting composition for the effective treatment of diseases of the stomach, as similarly desired by the applicants.

***Response to Arguments***

Applicant's arguments filed 09/30/03 have been fully considered.

Firstly, the applicant argued regarding the 35 U.S.C. §102(e) rejection over Akiyama ('773) stating, "Akiyama relates to a gastrointestinal mucosa-adherent solid preparation, which adheres to a particular site in the gastrointestinal tract. The lipids disclosed comprise a myriad of different types of lipids and no specific combination is

disclosed. Akiyama fails to teach each and every element of the claimed invention. Akiyama fails to teach each and every element of the present invention. "

Applicant's arguments with respect to claims 1-7, 9-15, 21-22, 25-29, 33, 34, 37-41 and 45 have been considered but are moot in view of the new ground(s) of rejection.

Secondly, the applicant argued regarding the 35 U.S.C. §103(a) of claims 8, 16-20, 23, 24, 30-32, 35, 36, 42-45 and 47 which were rejected over Akiyama *et al.* ('773) in view of Linder *et al.* (6,328,993) stating, "The references of record do not teach or suggest applicants' inventive subject matter as a whole recited in the claims. The examiner has failed to establish a prima facie case of obviousness against the presently rejected claims."

Applicant's arguments with respect to claims 8, 16-20, 23, 24, 30-32, 35, 36, 42-45 and 47 have been considered but are moot in view of the new ground(s) of rejection.

The rejection has now been reformulated as a 35 U.S.C. §103(a) rejection of claims 1, 2 and 4-47 over Akiyama ('773) in view of Shell ('389).

Akiyama, as delineated above, discloses a proton pump inhibitor formulation comprising a matrix containing a combination mixture of fatty acid esters, lipids and viscogenic agents, whereby lipids include saturated fatty acids or salts thereof, higher alcohols – cetyl alcohol, stearyl alcohol, fatty acid glycerol esters (mono-, di- or triglycerides), waxes, hydrocarbons – paraffin, microcrystalline wax and phospholipids)

in combination with pharmaceutically acceptable excipients. Various proton pump inhibitors include benzimidazole compounds such as lansoprazole, timoprazole, omeprazole and pantoprazole. The applicant's argument that a myriad of different lipids are taught, however only one is exemplified, is not persuasive since the art recognizes and teaches the generic concept of formulating an array of lipids to control the dissolution rates of the active ingredients. Furthermore, it is not essential that the prior art include multiple examples to demonstrate its particular teaching. It is sufficient that Akiyama recognizes the teaching of similar ingredients for the same field of endeavor and for a similarly intended purpose as the applicants. The instant claims require acid-labile active compounds and excipients, present in a matrix of a mixture of a fatty alcohol and a solid paraffin, wherein the active compound units are microspheres. The art teaches proton pump inhibitors with excipients in a matrix containing a combination mixture of fatty acid esters, lipids, viscogenic agents, higher and hydrocarbons, such as paraffin. Akiyama does not teach the active compound in microspheres. Shell resolves this only deficiency of Akiyama by teaching a gastro-retentive formulation in the form of tablets, capsules and microspheres, wherein the drugs that are delivered through these dosage forms include proton pump inhibitors, such as omeprazole. There is ample motivation provided by the art since each reference teaches treating diseases of the stomach using similar dosage forms and drugs for delivery. Therefore, the prior art clearly establishes a *prima facie* case of obviousness against the instant pending claims.

Furthermore, the applicants have not demonstrated any unexpected or surprising results that accrue from the instantly claimed ingredients. The prior art teaches a similar proton pump inhibitor formulation comprising similar ingredients for a functionally equivalent purpose as that desired by the applicants. Hence, the instant invention is rendered obvious and unpatentable over the prior art of record.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

*hns*
December 12, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600